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Outcome of cefazolin prophylaxis for total knee arthroplasty at an institution with high prevalence of methicillin-resistant *Staphylococcus aureus* infection[☆]

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SUMMARY

Objectives: The aim of this study was to evaluate the outcome of cefazolin prophylaxis for total knee arthroplasty (TKA) in a hospital with a high prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) infection.
Methods: Since July 1, 2006, we have applied a 'care bundle' to TKA to prevent surgical site infection (SSI) without using vancomycin as antimicrobial prophylaxis, in accordance with the 1999 Hospital Infection Control Practices Advisory Committee guidelines. All patients undergoing TKA from July 1, 2006 to September 30, 2009 were enrolled. We reviewed data on SSI collected prospectively as part of routine infection control surveillance.
Results: Of 1323 TKAs, an SSI developed in 14 (1.06%) cases, which is comparable to the percentage obtained in other previous reports. When stratified by the National Nosocomial Infection Surveillance risk index, SSI rates were 0.86% (8/926), 1.30% (5/384), and 7.69% (1/13) in risk categories 0, 1, and 2, respectively. Of 14 SSIs, four (29%) were classified as superficial incisional, two (14%) as deep incisional, and eight (57%) as organ-space SSI.
Conclusions: Our data suggest that antimicrobial prophylaxis using only cefazolin can maintain low SSI rates if other important infection management measures are employed, even where there is a high prevalence of MRSA infection.

1. Introduction

Surgical site infection (SSI) is a devastating complication, especially after implantation of prosthetic material. Because of the increasing prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) infections, there is a perceived need to use vancomycin for surgical antimicrobial prophylaxis in high-risk procedures (e.g., arthroplasty) and when endemic rates of SSI due to MRSA are high. However, 'high rates' of MRSA infection have not been defined and many effective measures exist for preventing SSI other than antimicrobial prophylaxis.[1]

MRSA accounts for over 60% of *S. aureus* nosocomial isolates in Korea, including in our institution – a tertiary care, university-affiliated 900-bed hospital.[2,3] Since 2006 we have applied a 'care bundle' to total knee arthroplasty (TKA) in order to prevent SSI without using vancomycin as antimicrobial prophylaxis, in accordance with the 1999 Hospital Infection Control Practices Advisory Committee guidelines.[4] In this study we evaluated the outcome of cefazolin prophylaxis for TKA and analyzed the risk factors for SSI in a hospital with a high endemic rate of MRSA infection.

2. Methods

2.1. Study setting and patients

Since July 1, 2006, we have applied a 'care bundle' to TKA to prevent SSI at Seoul National University Bundang Hospital, an academic tertiary care medical center. The care bundle consists of: (1) the use of an appropriate antiseptic agent for surgical scrub and skin preparation: aqueous solutions of 10% povidone–iodine and 2% chlorhexidine–alcohol are both considered appropriate; we used an aqueous solution of 10% povidone–iodine (Povidin, Sung

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Table 1
Surgical site infection rates after total knee arthroplasty, according to National Nosocomial Infection Surveillance risk index category

NNIS risk index category	No. of operations	No. of SSI	SSI rate[a] (95% CI)	KONIS[b] (2008)	NHSN[c] (2009)
0	926	8	0.86 (0.41–1.73)	0.93	0.58
1	384	5	1.30 (0.47–3.10)	1.65	0.99
2, 3	13	1	7.69 (0.01–35.42)	0	1.60
Total	1323	14	1.06 (0.61–1.79)	1.10	NA

SSI, surgical site infection; NNIS, National Nosocomial Infection Surveillance; CI, confidence interval; NA, not available.
[a] SSI rates are number of SSI cases per 100 operations; 95% confidence intervals were calculated by the modified Wald method.
[b] Korean Nosocomial Infections Surveillance System.[7]
[c] National Healthcare Safety Network.[8]

Kwang Pharm, Bucheon, Korea); (2) the adequate use of antimicrobial prophylaxis: timing (≤1 h before incision), choice (cefazolin), and duration of therapy (≤24 h after the procedure); (3) the following operating room characteristics: enough ventilation (≥15 times/h) using a HEPA filter, laminar air flow, and traffic control; and (4) reporting of compliance with the care to the attending surgeon every 3 months.

We performed a retrospective cohort study among patients undergoing TKA, from the initiation of the care bundle to September 30, 2009. We included all patients undergoing TKA during that period. These patients were identified using a surgical information recording system that routinely captures data on all surgical cases in both inpatient and outpatient settings in a prospective manner. We included only the type I surgical wound classification in our analysis; elective TKA is not applicable to patients with type II wound classifications.

2.2. Outcome assessment and patient follow-up

The primary outcome was development of any SSI within a year of surgery. All patients who underwent TKA were registered in the surgical information recording system. During admission, the surgical site was examined daily by the attending surgeon and the clinical information was recorded on a standardized record form. After discharge, patients were followed up in the outpatient clinic at 2 weeks, 6 weeks, 3 months, 6 months, and 1 year after surgery, as scheduled. Surgical site examinations were mainly performed by the attending surgeon, or if necessary by an infectious disease specialist. Clinical information (including the surgeon's description of the wound, diagnosis, and antibiotic prescriptions, etc.) was rechecked by an independent infection control practitioner in a prospective manner. If a patient failed to return for clinical follow-up, an infection control practitioner contacted the patient by telephone and asked him/her to complete a standardized form. During the follow-up period, patients suspected of having an SSI were identified by the surgeon or infection control practitioner using the criteria for SSI of the US Centers for Disease Control and Prevention (CDC).[4,5] Compliance with the care bundle and the follow-up rate were reported to the attending surgeon every 3 months. As a result, the 1-year follow-up rate was nearly 100% (99.6%, 1318/1323).

2.3. Statistical analyses

SSI rates were calculated according to the recommendations of the CDC.[4,5] Rates were stratified by the National Nosocomial Infection Surveillance (NNIS) risk index, categories 0–2. No patients were in NNIS category 3 because only type I wounds were included.[6] Differences between patients with SSI and without SSI were evaluated using the Chi-square test for categorical variables and the *t*-test for continuous variables. Univariate logistic regression was used to assess the association of selected variables with SSI. All analyses were performed using SPSS software version 17.0 (SPSS Inc, Chicago, IL, USA).

3. Results

3.1. Rates and characteristics of surgical site infection

From July 1, 2006 to September 30, 2009, 1323 TKAs were performed. SSIs occurred in 14 (1.06%) cases, including eight (0.60%) cases with prosthetic joint infection. When stratified by the NNIS risk index, SSI rates were 0.86% (8/926), 1.30% (5/384), and 7.69% (1/13) in risk categories 0, 1, and 2, respectively (Table 1).

Of the 14 procedures that resulted in diagnoses of infections, four (29%) resulted in SSIs that were classified as superficial incisional, two (14%) as deep incisional, and eight (57%) as organ-space SSI. Most (11/14, 79%) of the SSIs were early-onset infections (developing within 3 months of surgery).

In all of the cases with SSI, cefazolin was used as antimicrobial prophylaxis, given less than an hour before incision and discontinued within 24 h. Pathogens were identified in eight (57%) cases: four (50%) methicillin-sensitive *S. aureus* (MSSA), two (25%) MRSA, and two (25%) methicillin-resistant coagulase-negative staphylococci.

Cases with superficial incisional SSIs were treated with simple dressings or superficial wound revision, and short-term (≤2 weeks) oral antibiotics. Cases with deep incisional and organ-space SSIs received open or arthroscopic debridement with retention of the prosthesis, followed by a long course (at least 3 months) of intravenous antibiotics with or without subsequent oral agents. All 14 patients with SSI recovered from their infection without removal of the prosthesis, and there were no cases of relapse within at least 1 year of treatment.

3.2. Compliance with the care bundle

The preoperative antiseptic agents used in the surgical scrub and skin preparations were appropriate in all cases. In addition, all TKAs were performed in the same operating theatre with adequate ventilation (≥15 times/h) using HEPA filters, laminar air flow, and traffic control. In 98.7% (1306/1323) of the procedures, a prophylactic antimicrobial agent was administered within 1 h before incision. Cefazolin was used in 99.4% (1315/1323) of the cases and an antibiotic was used within 24 h of the procedure in 95.2% (1260/1323) of all the TKAs.

3.3. Risk factors for surgical site infection

The results of univariate analysis of the risk factors associated with SSI are presented in Table 2. No statistically significant risk factor for SSI was identified except for preoperative infection remote from the surgical site.

4. Discussion

In the present study the overall SSI rate after TKA was 1.06%. This is similar to the SSI rate after surgery in the 2008 Korean Nosocomial Infection Surveillance (KONIS) report, and higher than

Table 2
Univariate analysis: association of selected risk factors with surgical site infection following total knee arthroplasty

Factors	Patients		Univariate OR (95% CI)
	With SSI ($n = 14$)	Without SSI ($n = 1309$)	
Intrinsic, patient-related (preoperative)			
Age, >65 years	11 (79)	954 (73)	1.36 (0.38–4.92)
Gender, male	1 (7)	99 (8)	0.94 (0.12–7.26)
Preoperative hospital stay, ≥3 days	4 (29)	281 (21)	1.87 (0.56–6.28)
ASA score, ≥3	2 (14)	78 (6)	2.63 (0.58–11.96)
Diabetes	5 (36)	309 (24)	1.82 (0.61–5.47)
Obesity (BMI ≥25 kg/m^2)	12 (86)	929 (71)	2.45 (0.55–11.02)
Smoking	0	32 (2)	-
Immunosuppressive medication	0	17 (1)	-
Extrinsic, procedure-related (perioperative)			
Preoperative infection at another site	1 (7)	5 (0.4)	20.06 (2.19–183.87)
Operative characteristics			
General anesthesia	2 (14)	74 (6)	2.78 (0.61–12.66)
Duration of surgery >75th percentile	5 (36)	325 (25)	1.68 (0.56–5.06)
Repeated knee surgery	1 (7)	44 (3)	2.21 (0.28–17.28)
Antimicrobial prophylaxis			
Timing of administration of 1st dose ≤60 min before incision	14 (100)	1292 (99)	0.39 (0.02–6.85)
Choice, cefazolin	14 (100)	1301 (99)	0.19 (0.01–3.44)
Duration of therapy, ≤24 h	12 (86)	1248 (95)	0.29 (0.06–1.34)
Use of antibiotic-impregnated cement	7 (50)	713 (54)	0.84 (0.29–2.40)
Operating room characteristics			
Laminar flow	14 (100)	1309 (100)	-
HEPA filter in operation	14 (100)	1309 (100)	-
Ventilation, air exchange ≥15 times/h	14 (100)	1309 (100)	-

SSI, surgical site infection; OR, odds ratio; CI, confidence interval; ASA, American Society of Anesthesiologists; BMI, body mass index; HEPA, high-efficiency particulate air.

the rate in the 2009 National Healthcare Safety Network (NHSN) report .[7,8] However, active surveillance in this study mainly consisted of post-discharge surveillance by surgeon examination, and was carried out for all patients who received a TKA. Moreover both the microbiological findings and the clinical information (including surgeon examination of the wound, diagnosis, and antibiotic prescription) were rechecked by an independent infection control practitioner in a prospective manner. Bolon et al.,[9] showed that SSI rates were nearly doubled by active surveillance based on electronic data including diagnosis, prescription, etc. compared to routine surveillance by microbiological results alone. Also, as indicated by Huotari and Lyytikainen,[10] post-discharge surveillance greatly impacts on the rate of SSI detected after orthopedic surgery. Therefore we are unlikely to have missed any case with SSI, and the SSI rate obtained was either similar to or lower than those obtained in the 2009 NHSN and 2008 KONIS and other reports from various countries.[7,8,10–12]

Recently, as infections due to MRSA have increased, the opinion has emerged that vancomycin should be used as antimicrobial prophylaxis in special circumstances.[4] However, there is controversy regarding in which situations vancomycin should be used. There is no consensus about what constitutes ‘high prevalence’ of methicillin resistance, and there have been few prospective randomized controlled studies comparing glycopeptides (± beta-lactam) and beta-lactam antimicrobials as antimicrobial prophylaxis. Potential adverse effects of the use of vancomycin as antimicrobial prophylaxis (emergence of resistance, drug toxicity, high cost, and so forth) should be considered.

Other than making the appropriate choice of antimicrobial prophylaxis, many important measures can be taken to prevent SSI, such as appropriate skin preparation, adequate use of antimicrobial prophylaxis with regard to indication, timing, and duration of therapy, and adequate ventilation with a HEPA filter, laminar air flow, and traffic control in the operating room.[1] In view of this we thought it was more important to abide by infection management guidelines before using vancomycin, which remains controversial as antimicrobial prophylaxis. We applied a care bundle to TKA, and compliance was regularly reported to the attending surgical team. As a result, compliance was over 95% for all items and we were able to achieve a low SSI rate without using vancomycin.

This study has a few limitations. First, it was not a prospective comparative study and so has the disadvantage that we could not directly compare the effects of vancomycin and cefazolin. Second, all 14 cases with SSI in our study were completely compliant with the care bundle and in four (50%) of the eight patients for whom the cause of infection was identified, it was due to methicillin-resistant staphylococci. Hence, the care bundle alone does not guarantee the lowest SSI rates. Therefore, the use of vancomycin selectively in certain patients has the potential to reduce SSI, and further research on this is called for. Third, we used an aqueous solution of 10% povidone–iodine as antiseptic agent, in accordance with the 1999 Hospital Infection Control Practices Advisory Committee guidelines.[4] However, recent work has demonstrated significant reductions of SSI after clean-contaminated surgery, and of bloodstream infections after vascular catheter insertion, when a chlorhexidine-based agent was used for antisepsis.[13,14] Although the effect of chlorhexidine-based antisepsis has not been carefully compared with that of povidone–iodine in clean surgery (including in arthroplasty), antisepsis with chlorhexidine–alcohol could result in a significant clinical benefit. Lastly, since infection due to community-associated MRSA (CA-MRSA) is rare in Korea,[2] the SSI rate after surgery in regions in which CA-MRSA is prevalent may be different from that obtained in this study.

Nevertheless, our data suggest that even where there is a high prevalence and high incidence of MRSA infection, antimicrobial prophylaxis in TKA using only cefazolin can maintain low SSI rates after surgery if other important infection management measures are employed.

Conflict of interest: No author received financial support. There are no potential conflicts of interest for any authors.

Ethical approval: This study was approved by the institutional review board of Seoul National University Bundang Hospital.

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